AD_____

ARMY PROJECT ORDER NO: 89PP9952

TITLE: DEVELOPMENT AND USE OF A SWINE MODEL FOR EVALUATING ANESTHETIC AGENTS AND DEVICES

SUBTITLE: The Effects of Ketamine and Thiopental on Myocardial Contractility and Function in Hypovolemic Swine

PRINCIPAL INVESTIGATOR: Charles P. Kingsley, M.D.
Sanford M. Silverman, M.D.

CONTRACTING ORGANIZATION: U.S. Army Health Services Command
Brooke Army Medical Center
Fort Sam Houston, TX 78234-6200

REPORT DATE: September 1, 1990

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21702-5012

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release; distribution unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION U.S. Army Health Services Command 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) Brooke Army Medical Center Fort Sam Houston, TX 78234-6200	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION U.S. Army Medical Research & Development Command 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER Army Project Order No. 89PP9952
8c. ADDRESS (City, State, and ZIP Code) Fort Detrick Frederick, Maryland 21702-5012	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 61102A; PROJECT NO. 3M1 61102BS13 ✓; TASK NO. ZZ; WORK UNIT ACCESSION NO. 081

11. TITLE (Include Security Classification)
Development and Use of a Swine Model for Evaluating Anesthetic Agents and Devices

12. PERSONAL AUTHOR(S)
Charles P. Kingsley, M.D., Sanford M. Silverman, M.D.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Final Report	FROM 7/15/89 TO 8/14/90	1990 September 1	26

16. SUPPLEMENTARY NOTATION
Subtitle: The Effects of Ketamine and Thiopental on Myocardial Contractility and Function in Hypovolemic Swine

17. COSATI CODES		
FIELD	GROUP	SUB-GROUP
06	12	

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
Swine; Anesthesia, ~~RA 11~~

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Ketamine has been advocated for the induction of anesthesia in the acutely hypovolemic patient because of its ability to preserve blood pressure which is mediated by catecholamine induced vasoconstriction. Thiopental causes a decrease in blood pressure and vasodilation, which are exacerbated during hypovolemia. The effects of anesthetic induction doses of Ketamine and thiopental were evaluated in a hypovolemic swine model. Sixteen acutely instrumented swine were mechanically ventilated with N_2O (70%) and O_2 (30%) and hemorrhaged to a mean arterial blood pressure of 40mm Hg. After 15 minutes of stabilization, ketamine (6 mg/kg) or thiopental (6 mg/kg) was administered as an intravenous bolus to simulate the induction of anesthesia. Hemodynamic measurements from a polmonary artery catheter were made at baseline and hemorrhage states, and 1, 5, 15, and 30 minutes after drug administration. Cardiodynamics consisting of myocardial contractility (Ees) and left ventricular function were assessed from the end-systolic pressure-dimension relationship (ESPDR) and pressure-dimension (PD) loops respectively. These cardiodynamics were generated from sonomicrometer crystals and a pressure transducer placed in the left ventricle.

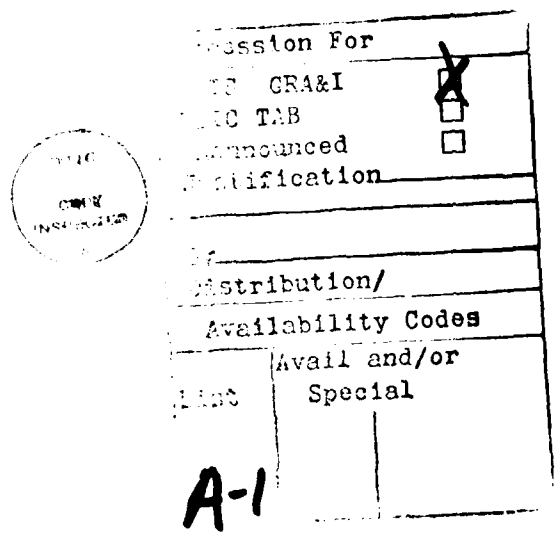
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION	
☐ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	Unclassified	
22a. NAME OF RESPONSIBLE INDIVIDUAL Mrs. Virginia M. Miller	22b. TELEPHONE (Include Area Code) (301) 663-7325	22c. OFFICE SYMBOL SGRD-RMI-S

DD Form 1473, JUN 86 *Previous editions are obsolete* SECURITY CLASSIFICATION OF THIS PAGE

FOREWORD

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

Supported in part with funds and equipment through U.S. Army Medical Research and Development Command and U.S. Army Biomedical Research and Development Laboratory.



ABSTRACT

Ketamine has been advocated for the induction of anesthesia in the acutely hypovolemic patient because of its ability to preserve blood pressure which is mediated by catecholamine induced vasoconstriction. Thiopental causes a decrease in blood pressure and vasodilation, which are exacerbated during hypovolemia. The effects of anesthetic induction doses of ketamine and thiopental were evaluated in a hypovolemic swine model. Sixteen acutely instrumented swine were mechanically ventilated with N_2O (70%) and O_2 (30%) and hemorrhaged to a mean arterial blood pressure of 40 mm Hg. After 15 minutes of stabilization, ketamine (6 mg/kg) or thiopental (6 mg/kg) was administered as an intravenous bolus to simulate the induction of anesthesia. Hemodynamic measurements from a pulmonary artery catheter were made at baseline and hemorrhage states, and 1, 5, 15, and 30 minutes after drug administration. Cardiodynamics consisting of myocardial contractility (Ees) and left ventricular function were assessed from the end-systolic pressure-dimension relationship (ESPDR) and pressure-dimension (PD) loops respectively. These cardiodynamics were generated from sonomicrometer crystals and a pressure transducer placed in the left ventricle.

Thiopental but not ketamine significantly depressed Ees ($P < 0.05$). Both anesthetics significantly increased end-diastolic dimension (Ded) and end-systolic dimension (Des). Thiopental increased mean pulmonary artery pressure (MPAP) and pulmonary vascular resistance (PVR). Ketamine increased PVR. Ketamine but not thiopental decreased cardiac index (CI) and increased systemic vascular resistance (SVR). Pulmonary capillary wedge pressure (PCWP) was significantly elevated by thiopental but not by ketamine. The PD loops obtained demonstrate similar pressure and dimension shifts for ketamine and thiopental, returning to their hemorrhaged state by 5 minutes.

Both ketamine and thiopental depress cardiac function in hypovolemic swine, but thiopental has a greater myocardial depressant effect. The ESPDR and PD loop, together with hemodynamic measurements allow a thorough evaluation of cardiac function coupled to the vascular system. The effects of induction doses of various anesthetics may be ascertained utilizing this methodology.

INTRODUCTION

Anesthetic induction in the acutely traumatized , hypovolemic patient is difficult because of the need to balance adequate anesthesia with hemodynamic stability. Intraoperative awareness from inadequate levels of anesthesia is a recognized post-operative complaint of trauma patients.[1] The extent of hypovolemia, although usually corrected prior to the induction of anesthesia, may not be recognized. Trauma patients may present for emergency surgery awake and responsive with stable vital signs, their hypovolemia masked by elevated sympathetic tone. In addition, the urgency of surgery may not allow sufficient time for fluid resuscitation. Therefore, it may be necessary to induce anesthesia in relatively hypovolemic patients.

Thiopental is the most commonly used intravenous agent for anesthetic induction because of its rapid onset. However, it may cause depression of the myocardium and peripheral vasculature.[2,3,4] Ketamine has been advocated for anesthetic induction for the hypovolemic patient because of its ability to maintain blood pressure and heart rate through its central sympathomimetic effect with the concomitant release of endogenous catecholamines.[5-6] However, ketamine can also produce direct myocardial depression. [7,8,9]

Cardiac output is a function of four basic parameters: preload, afterload, heart rate , and contractility. It has been demonstrated in animals that depression of cardiac function during shock-like states may be attributed to depression of contractility as well as preload.[10] Ketamine and thiopental have been studied utilizing $(dP/dt)_{max}$,[8] a preload dependent index of contractility. Since both preload and

afterload vary rapidly in shock-like states, this index could be inaccurate. Therefore , a measurement of contractility independent of loading conditions and heart rate would be preferable in a hypovolemic model.

The end-systolic pressure-volume relationship (ESPVR) yields a measure of contractility (Ees) that is independent of heart rate and loading conditions.[11] Together, the ESPVR and the pressure-volume loop area provide measures of : 1) myocardial oxygen consumption 2) coupling of the heart and peripheral vasculature 3) the efficiency of the heart as a pump.[12] A variation of this concept, the end-systolic pressure-dimension relationship (ESPDR) has been used successfully in vivo to assess effects of anesthetics on myocardial function.[13-14] The ESPDR has also been used to assess contractility in animal shock models.[10,15] Therefore, the effect of anesthetics on cardiac function may be assessed by the ESPDR during rapid changes in peripheral vascular loading conditions, as in acute hemorrhage.

The purpose of this study was to assess the effects of anesthetic induction doses of ketamine and thiopental on myocardial contractility and function utilizing the ESPDR in a hypovolemic swine model. Prior studies[15-16] have examined the hemodynamic effects of these agents on hypovolemic swine. However, the effects of these anesthetics have not been evaluated in a hypovolemic animal model utilizing the ESPDR. This information may be useful in evaluating the response of hypovolemic patients to anesthetic induction with these agents.

METHODS

Under an approved animal use protocol, 16 Yorkshire swine weighing 18-23 kg were anesthetized with halothane in a mixture of N_2O and O_2, and their tracheas were intubated. Atracurium was used for muscle relaxation. Anesthesia was maintained with halothane, N_2O, and O_2. Ventilation was controlled to maintain normocarbia. End-tidal CO_2 and halothane concentration were monitored continuously with an Ohmeda 6000 gas analyzer. Animals were ventilated with an Air Shields ventilator to maintain end-tidal

CO_2 between 30 and 35 mm Hg. A 20 gauge catheter and 8.5 Fr introducer were placed via cutdown in the femoral artery and right internal jugular vein respectively. An intravenous infusion of lactated ringers solution (6 ml/kg-hr) was given through the jugular line. A 7 fr pulmonary artery catheter(PAC) (American Edwards Laboratories) was floated to the the wedge position for measurement of cardiac output (CO), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), and central venous pressure (CVP). Cardiac output was measured in triplicate (5 ml of 0.9% NaCl at room temperature) using an Edwards Model 9520A analog computer. Cardiac index (CI), pulmonary vascular resistance (PVR), and systemic vascular resistance (SVR) were calculated from the PAC. Oxygen saturation via pulse oximetry (Ohmeda Biox 3700) was monitored along with the ECG. Temperature was maintained with a heating blanket and the use of humidified inspired gases.

Instrumentation

Through a left subcostal incision, the animals were splenectomized to minimize the effects of autotransfusion, which is a physiologic response to hemorrhage in swine.[17] A median sternotomy was then performed and an umbilical tape with snare was placed around the inferior vena cava (IVC) to vary preload. The heart was suspended in the pericardial sac and 2 sonomicrometer crystals (Triton Technology, San Diego, CA) were implanted in the anterior and posterior walls of the left ventricle (LV). Signals were amplified using a polygraph recorder, with analog to digital conversion at 200 Hz and analyzed on an IBM-AT compatible computer. A 5 mm hi-fidelty pressure transducer (Konigsberg Instruments, Pasadena, CA) was inserted through the apex of the left ventricle for measurement of LV pressure.

Experimental Protocol

At the conclusion of surgery, the incisions were approximated, halothane was discontinued, and anesthesia was maintained with N_2O (70%) , O_2 (30%), and atracurium. Periodic arterial blood gas analysis confirmed the end-tidal CO_2 analysis and allowed maintenance of normal acid-base status and PO_2 greater than 100 mm hg.

Generation of pressure-dimension loops and calculation of Ees

When the end-tidal halothane concentration was less than 0.1%, baseline control (BC) hemodynamic measurements were obtained. Pressure-dimension (PD) loops were generated by occluding the IVC. This caused a sudden drop in left ventricular pressure and dimension over a 10 second recording period. IVC occlusion ceased immediately after the recording period. Ventilation was discontinued during occlusion to remove respiratory artifact from the PD signal. The ESPDR was determined by fitting a least squares line to the seven end-systolic points exhibiting the greatest combined pressure and dimension drop during an IVC occlusion. The slope of this line (Ees) is a measure of contractility (fig 1). End-diastolic dimension (Ded) and end-systolic dimension (Des) were also recorded.

After baseline control data were obtained, the animals were hemorrhaged in 50 ml aliquots to a mean arterial pressure of 40 mm hg. The swine were left undisturbed for 10-15 minutes to allow for a new steady-state. Repeat hemodynamic measurements and PD loops were obtained at this hemorrhaged state (H). Thiopental (6 mg/kg) or ketamine (6 mg/kg) was given as an intravenous bolus to simulate the induction of anesthesia and replicate hemodynamic data and PD loops were obtained at 1,5,15, and 30 minutes after injection (H1, H5, H15, H30 respectively). After completion of the experiment, animals were sacrificed via lethal intravenous injection (T-61 euthanasia solution).

Cardiodynamic (Ees, Ded, and Des) and hemodynamic data were analyzed with ANOVA for repeated measures testing followed by a Fischer Least-Significant-Difference test for paired comparisons. A $p < 0.05$ was considered statistically significant.

RESULTS

The mean weight and hemorrhaged blood volume were similar for each group and are shown in table 1. All animals demonstrated appropriate physiologic responses to hemorrhage with increased heart rate and decreased MAP.

Thiopental group

Hemodynamic parameters for thiopental are shown in table 2. Cardiodynamic parameters obtained from the ESPDR and the PD loops are shown in table 3. Figure 2 shows the PD loops at baseline control, hemorrhage, and one minute after administration of thiopental. Statistically significant increases in HR and Ees were observed after hemorrhage. MAP, PCWP, CI, Ded, and Des significantly decreased after hemorrhage. Ees was significantly depressed by thiopental at H1 and H5. Thiopental significantly increased PVR and MPAP at H1,H5, H15 and MPAP at H30. PCWP was significantly increased at H1 through H30. Ded and Des were significantly increased by thiopental at H1. HR and SVR were not significantly altered by thiopental. MAP was significantly increased at H5.

Ketamine group

Hemodynamic and cardiodynamic parameters for ketamine are presented in tables 4 and 5 respectively. Figure 3 shows the PD loops at baseline control, hemorrhage, and one minute after administration of ketamine. Statistically significant increases in HR and Ees were observed after hemorrhage. CI, Ded, and Des were significantly decreased after hemorrhage. Ketamine did not significantly alter Ees, MAP, MPAP, HR or PCWP. Ketamine

significantly increased Ded, Des, PVR, and SVR at H1 and PVR at H5. Ketamine significantly depressed CI and significantly increased SVR at H1.

DISCUSSION

The results of this study indicate that in hypovolemic swine, myocardial contractility (Ees) as assessed by the end-systolic pressure-dimension relationship (ESPDR) is significantly depressed by thiopental but not by ketamine. Both anesthetics cause a transient depression of Ees and cardiac function. Ees recovers to the hemorrhaged state by 15 minutes after thiopental administration while the PD loops generated for both agents recover by 5 minutes.

The use of ketamine and thiopental for anesthetic induction in emergency surgery is well established. These agents given intravenously in the appropriate doses act rapidly to produce anesthesia. The doses used in this study have been determined to be anesthetic in swine.[16] However, these anesthetics have different effects on cardiovascular function during normovolemia and hypovolemia. Thiopental causes depression of the myocardium and peripheral vasculature[2-4,8] and has similar effects during hypovolemia. [15,16] Ketamine increases heart rate, mean arterial pressure, and cardiac output when administered to normovolemic animals[7] and humans.[6] However, during hypovolemia these parameters decrease.[15,16]

Myocardial contractility determines the strength of cardiac contraction. Biochemically it represents the number and tension-generating capacity of the rigor complexes and maximal rate of energy liberation in the interactions between contractile proteins and ATP.[18] Since loading conditions vary in hemorrhagic shock-like states, the use of a load-insensitive measure of contractility (Ees) is justified. Contractility however, is only one determinant of cardiac function. The ESPDR and PD loops provide an assessment of the heart's coupling to the peripheral vascular system. The downward and leftward shift of the PD loop with hemorrhage indicate decreased LV pressure, Des, and Ded. However, increased

contractility as reflected by an increased Ees is present as a result of physiologic sympathetic stimulation. With anesthetic administration, the PV loops shift further downward and to the right. Ees is depressed indicating depressed contractility and a concomitant increase in Ded and Des is seen, reflecting depression of overall ventricular function. Ees was significantly depressed by thiopental but not by ketamine. The PD loops return to the hemorrhaged state by 5 minutes after administration of both anesthetics (figs 2-3).

The results indicate that thiopental significantly depresses Ees but not CI, MAP, or HR. Ketamine did not significantly depress Ees but did significantly depress CI at 1 minute. Ketamine also significantly increased SVR at 1 minute, which would account for the decrease in CI. MAP and HR were not altered by either anesthetic except by thiopental, which increased MAP at 5 minutes. However, significant changes in these variables may have occurred before 1 minute. A depression of MAP and HR was observed immediately *following injection* of thiopental and ketamine, which was maximal at approximately 30 seconds but rapidly recovered by one minute. Generation of the ESPDR required at least 10 seconds and replicate CO measurements 60 seconds. Therefore, obtaining data prior to one minute was impossible. Consequently, data was collected at 1, 5, 15, and 30 minutes. It is possible that CI, MAP, and HR were significantly depressed sometime less than 1 minute. Although MAP and HR are not depressed by either anesthetic, cardiac function as demonstrated by the PD loops is (figs 2-3). Ded and Des are significantly increased by both anesthetics indicating decreased ventricular emptying. Thiopental but not ketamine increased PCWP without increasing CI, indicating reduced ventricular compliance and function.

Our results are similar to Weiskopf et al [16] and show that ketamine and thiopental produce depression when both are given at similar anesthetic doses. However, our results indicate thiopental may have more depressing effects on the myocardium than ketamine. This would agree with Horowitz[8] who found that thiopental but not ketamine decreased $(dP/dt)_{max}$ in dogs, without significant changes in LV pressure.

The increase in MPAP by thiopental may have been secondary to decreased LV compliance, reflected by the increase in PCWP, transmitted back to the pulmonary circulation. Another reason for increases in MPAP and PVR may have been a decrease in the level of anesthesia resulting from the rapid redistribution of thiopental from the central nervous system. However, ketamine did not increase PCWP or MPAP but did increase PVR at 1 and 15 minutes. Ketamine has been shown to increase PVR in humans[19]. This increase may have been due to light anesthesia as well. Ketamine's release of catecholamines with concomitant peripheral vasoconstriction would account for the observed increase in SVR.

In conclusion, we have shown that both ketamine and thiopental depress myocardial function in a hypovolemic swine model, but thiopental appears to be more of a myocardial depressant. Both anesthetics depress ventricular function with shifts of the PD relationship and increases in Ded and Des. Cardiac function returns to the hemorrhaged state by 5 minutes. Contractility is not the sole determinant of cardiac function and may not be adequate in assessing ventricular function in hypovolemic states. Assessment of the heart's interaction with the vascular system utilizing the ESPDR and PD loops may be more useful in evaluating the effects of anesthetics in a hypovolemic model.

Table 1
Mean weight and hemorrhaged blood volume
mean ± SD

GROUP

	Thiopental	Ketamine
weight (kg)	19.8 ± 1.8	20.1 ± 1.7
Bled volume (ml)	154 ± 97	156 ± 61
Bleed/kg (ml/kg)	7.8 ± 4.8	7.8 ± 3.1

Table 2
Hemodynamics - Thiopental
mean +/- SD

Time (min)	BC	H	H1	H5	H15	H30
MAP	64*	53	52	63*	59	61
(mm Hg)	7	6	15	9	11	9
HR	115*	134	130	133	124	129
	19	21	22	12	13	16
CI	3.1*	2.4	2.2	2.4	2.2	2.3
($l/min-m^2$)	0.5	0.7	0.6	0.7	0.4	0.5
MPAP	18	16	20*	21*	19*	19*
(mm Hg)	5	4	5	7	7	5
SVR	31	35	34	39	39	41*
(mm Hg/l/min)	7	9	8	7	7	10
PVR	6.2	8.0	11.2*	10.6*	9.9*	10.0
(mm Hg/l/min	3.1	4.1	6.0	6.0	5.3	5.0
PCWP	6.0*	4.5	5.9*	5.6*	6.0*	5.8*
(mm Hg)	2.7	1.8	3.0	2.0	1.6	1.8

* $P < 0.05$ when compared to hemorrhage (H)

Table 3
Cardiodynamics - Thiopental
mean +/- SD

Time (min)	BC	H	H1	H5	H15	H30
Ees	14.7*	24.8	17.5*	17.8*	22.4	23.5
(mm hg/mm)	6.0	12.5	10.8	6.1	12.3	10.7
Ded	26.0*	23.8	26.2*	24.7	24.9	24.9
(mm)	5.7	5.6	6.4	7.0	6.4	6.8
Des	20.5*	19.4	22.6*	19.9	20.1	20.1
(mm)	6.4	6.1	5.8	6.6	5.8	6.5

* $P < 0.05$ when compared to hemorrhage (H)

Table 4
Hemodynamics - Ketamine
mean +/- SD

Time (min)	BC	H	H1	H5	H15	H30
MAP	58	52	54	55	57	60
(mm Hg)	7	2	15	11	11	14
HR	107*	127	118	121	125	125
	14	26	30	34	38	35
CI	2.7*	2.2	1.9*	2.1	2.1	2.4
($l/min-m^2$)	0.6	0.6	0.4	0.4	0.4	0.5
MPAP	17	15	16	16	16	16
(mm Hg)	4	3	6	4	6	5
SVR	32	34	39*	37	38	37
(mm Hg/l-min)	11	11	13	10	11	11
PVR	5.9	5.9	8.0*	7.2	8.0*	6.5
(mm Hg/l-min)	2.8	4.1	4.7	3.5	4.8	3.1
PCWP	7.9	6.8	6.5	6.5	6.5	6.6
(mm Hg)	3.0	2.1	1.7	1.6	1.6	1.9

* $P < 0.05$ when compared to hemorrhage (H)

Table 5
Cardiodynamics - Ketamine
Mean +/- SD

Time (min)	BC	H	H1	H5	H15	H30
Ees	14.0*	23.7	17.4	20.7	21.6	24.1
(mm Hg/mm)	5.7	11.0	12.1	10.6	9.9	14.4
Ded	28.7*	26.1	27.9*	27.1	26.6	26.6
(mm)	6.7	7.4	7.1	7.5	7.7	7.6
Des	23.8*	22.3	24.1*	23.2	22.5	22.4
(mm)	6.9	8.0	7.6	7.6	8.0	7.9

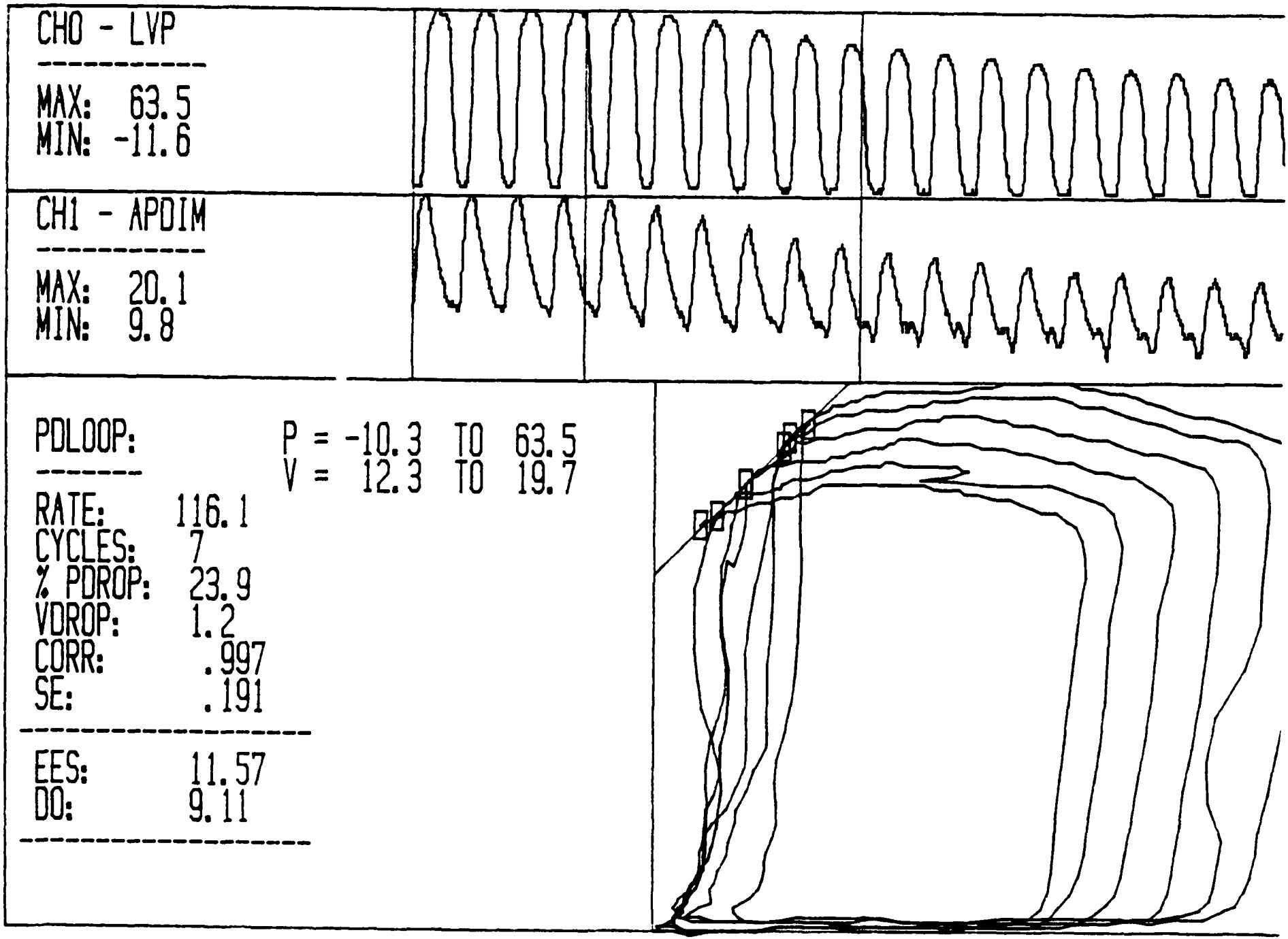
* $P < 0.05$ when compared to hemorrhage (H)

ACKNOWLEDGEMENT

Special thanks to JM Farooqui for providing a thorough data analysis and to Dan Williams for his expertise in handling the animals and trouble shooting equipment in the laboratory.

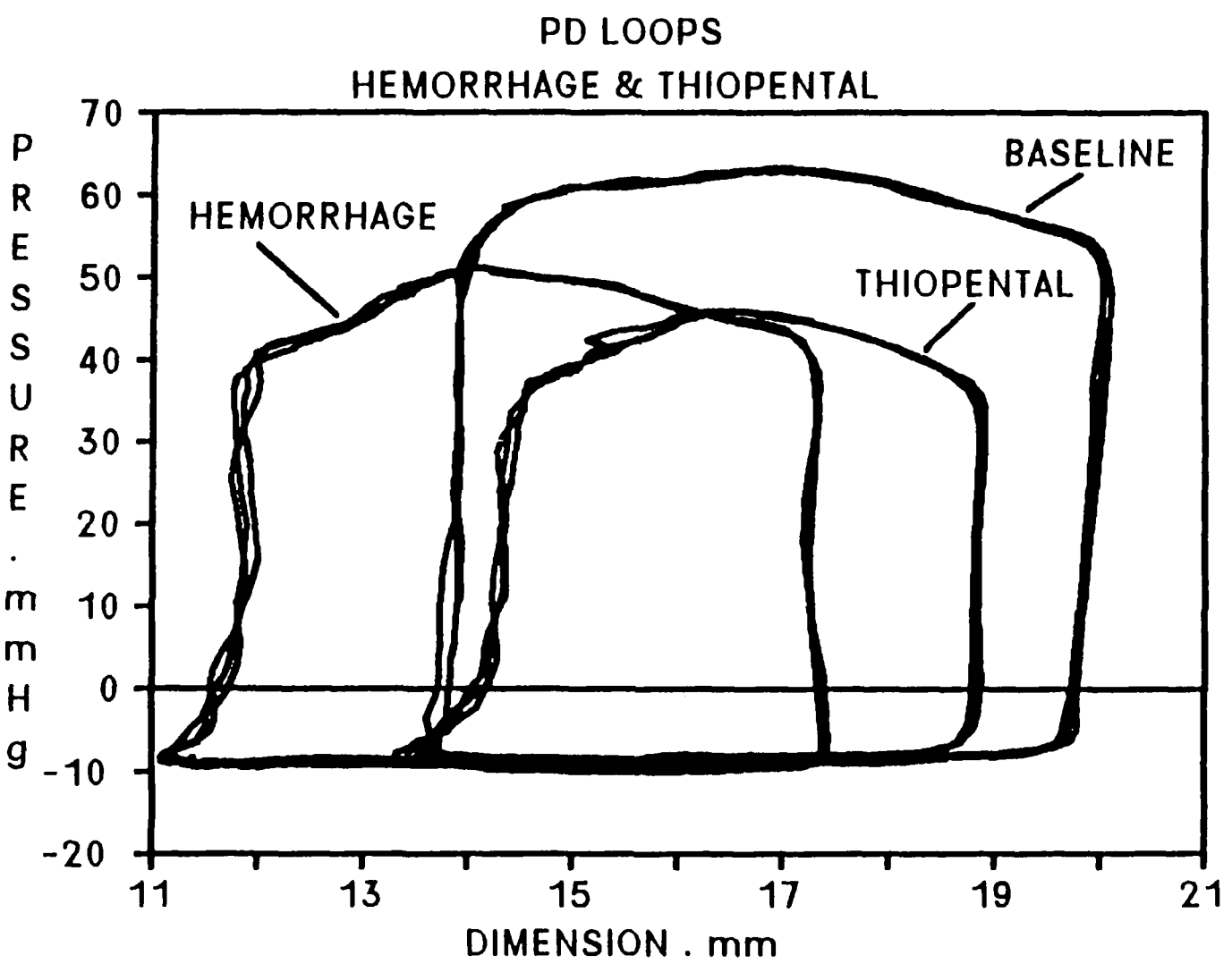
LEGEND

Figure 1: Generation of the end-systolic pressure-dimension relationship and calculation of contractility (Ees).


CH0 - LVP
MAX: 63.5
MIN: -11.6
CH1 - APDIM
MAX: 20.1
MIN: 9.8
PDLOOP:
P = -10.3 TO 63.5
V = 12.3 TO 19.7
RATE: 116.1
CYCLES: 7
% PDROP: 23.9
VDROP: 1.2
CORR: .997
SE: .191
EES: 11.57
DO: 9.11

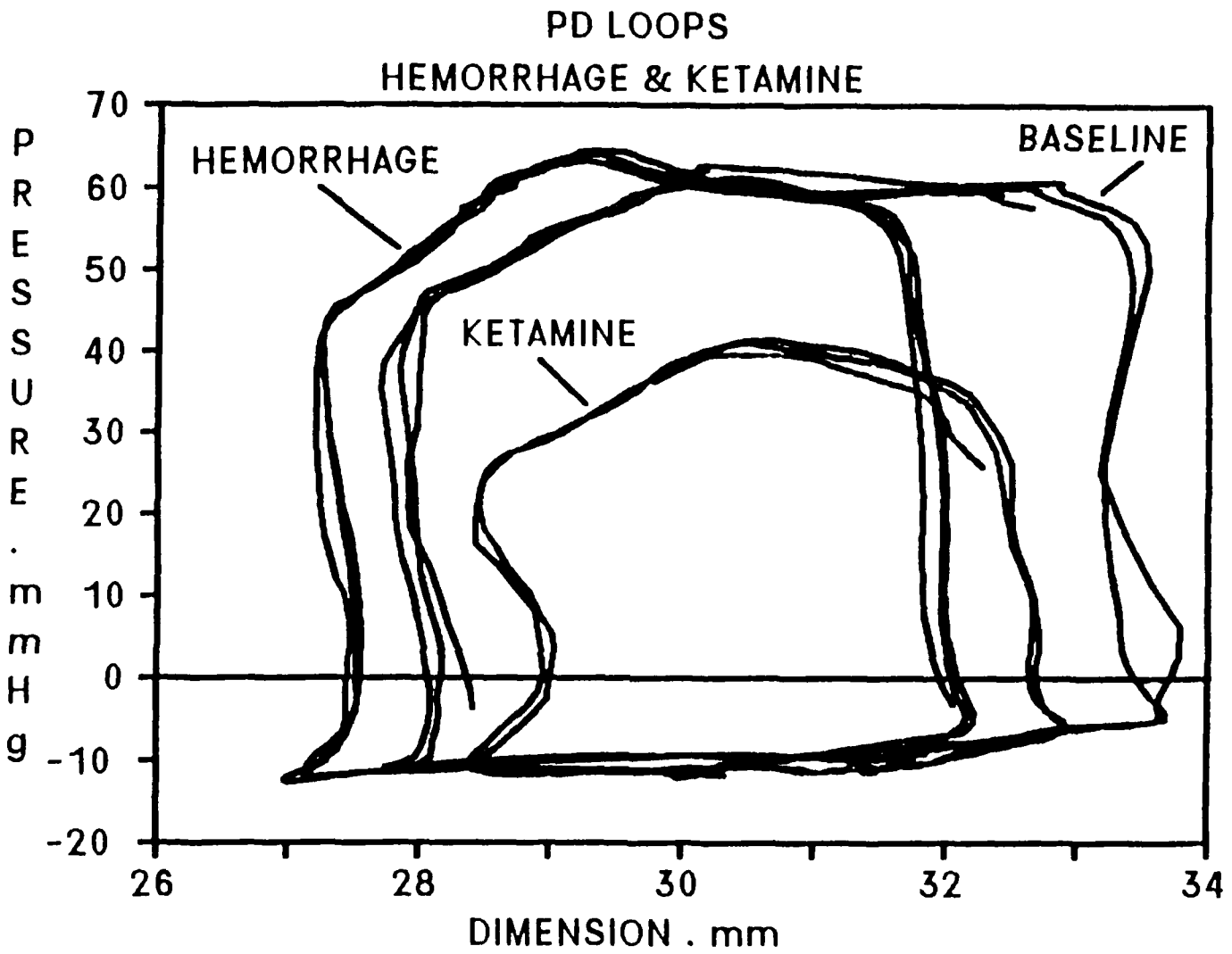
LEGEND

Figure 2: Pressure-dimension loops for thiopental at baseline, hemorrhage, and one minute after drug administration.


PD LOOPS
HEMORRHAGE & THIOPENTAL
BASELINE
HEMORRHAGE
THIOPENTAL
PRESSURE . mmHg
70
60
50
40
30
20
10
0
-10
-20
11
13
15
17
19
21
DIMENSION . mm

LEGEND

Figure 3: Pressure-dimension loops for ketamine at baseline, hemorrhage, and one minute after drug administration.


PD LOOPS
HEMORRHAGE & KETAMINE
HEMORRHAGE
BASELINE
KETAMINE
PRESSURE . mmHg
70
60
50
40
30
20
10
0
-10
-20
26
28
30
32
34
DIMENSION . mm

REFERENCES

[1] Bogetz MS and Katz JD: Recall of surgery for major trauma. Anesthesiology 61: 61-9, 1984.

[2] Bernards C, Marrone B, PrianoL: Effect of anesthetic induction agents on baroreceptor function. Anesthesiology 63: A31, 1985.

[3] Etsten B and Li TH: Hemodynamic changes during thiopental anesthesia in humans: Cardiac output, Stroke volume, total peripheral resistance, and intrathoracic blood volume. J Clin Invest 34: 500-510, 1955.

[4] Eckstein JW, Hamilton WK, McCammond JM: The effect of thiopental on peripheral venous tone. Anesthesiology 22: 525-528, 1964.

[5] Idvall J et al: Ketamine infusion: Pharmacokinetics and clinical effects. Br. J. Anaesth. 51: 1167-72, 1979.

[6] Tweed WA et al: Circulatory responses to ketamine anesthesia. Anesthesiology 37: 613-19, 1972.

[7] Traber DL et al: Effects of CL 1848C, a new dissociative anesthetic, on the canine cardiovascular and respiratory systems. J. Pharmacol. Exp. Ther. 175: 395-403, 1970.

[8] Horowitz LD: Effects of intravenous anesthetic agents on left ventricular function in dogs. Am. J. Physiology 232: (1), H44-8, 1977.

[9] Diaz FA, Bianco JA, Bello A, Beer N, Uelarde H, Izquierdo JP, Jaen R: Effects of ketamine on canine cardiovascular function. Br. J. Anaesth 48: 941-945, 1976.

[10] Goldfarb RD: Evaluation of ventricular performance in shock. Circulatory shock 15: 281-301, 1985.

[11] Suga H, Sagawa K, Shoukas AA: Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and

effects of epinephrine and heart rate on the ratio. Circ. Research, 32: 314-22,1973.

12 Burkhoff D and Sagawa K: Ventricular efficiency predicted by an analytical model. AM. J. Physiol, 250 (Regulatory Integrative Comp. Physiol. 19): R1021-R1027, 1986.

13 Van Trigt P et al: Myocardial depression by anesthetic agents (halothane, enflurane, and nitrous oxide): quantitation based on end-systolic pressure-dimension relations. Am. J. Cardiol , 53: 243-47, 1984.

14 Coetzee A et al: Effects of various propofol plasma concentrations on regional myocardial contractility and left ventricular afterload. Anesth. Analg., 69: 473-83, 1989.

15 Olson KW, Kingsley CP, Ward JA, Hemodynamic consequences of anesthetic induction with etomidate in hypovolemic swine. (unpublished data)

16 Weiskopf RB et al, Cardiovascular and metabolic sequelae of inducing anesthesia with ketamine or thiopental in hypovolemic swine. Anesthesiology 60: 214-219, 1984.

17 Bustad LR, McKlellan RO, eds. Swine in Biomedical Research. Richland, Washington, Battelle Memorial Institute, Pacific Northwest Laboratory, 1966.

18 Katz AM: Physiology of the Heart. Raven Press, New York: 1977.

19 Spotoft H, et al. The cardiovascular effects of ketamine used for induction of anaesthesia in patients with valvular heart disease. Canad. Anaesth. Soc. J., 26: 463-467, 1979.